

REMARKS

Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, and 116-130 are pending and under consideration. Applicants cancel, without prejudice, claim 124. Applicants reserve the right to prosecute claims of similar or differing scope.

1. Information Disclosure Statement

Applicants note that the Information Disclosure Statements filed 25 July 2005 and 21 September 2005 have been received and considered. Applicants wish to bring to the Examiner's attention co-pending U.S. application 10/016,969, assigned to Amylin Pharmaceuticals, Inc.

2. Withdrawn Objections and/or Rejections

Applicants note with appreciation that the rejection of claims 13, 21, 23, 33, 45, 87, 92, 93, and 122 under 35 U.S.C. 112, second paragraph, has been withdrawn.

Applicants note with appreciation that the rejection of claims 23, 89, 102-105, 108, 111, and 118 under 35 U.S.C. 102(b) has been withdrawn.

3. Claim Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 109, 112, and 119 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to enable one of skill in the art to practice the claimed invention. Applicants traverse this rejection to the extent it is maintained in light of the amended claims.

The Examiner states that “the instant specification fails to demonstrate that PYY affects hyperlipidemia or hyperlipoproteinemia” (page 4 of the October 17, 2005 Office Action). The Examiner appears to be requiring that Applicants provide a working example demonstrating that PYY treats hyperlipidemia or hyperlipoproteinemia. Applicants have presented working examples demonstrating the ability of PYY to affect glucose responsiveness, and have pointed to several places in the specification and claims as filed which provide enabling support for the use of a PYY agonist or biologically active fragment thereof effective to treat a disease associated with glucose metabolism. For example, the specification clearly states “The method may be used for treating a disease that is associated with a condition such as insulin resistance, glucose intolerance or glucose non-responsiveness, hyperglycemia, obesity, hyperlipidemia and

hyperlipoproteinemia in an animal” (page 5, lines 34-36 of the specification). Dosage of the compound is provided, for example, on page 29, lines 30-34. Therefore, Applicants have stated that the PYY or PYY agonist will treat a disease associated with altered glucose metabolism, and have provided dosages, allowing one of ordinary skill in the art to make and use the claimed invention. The Examiner acknowledges that she does not deny an association between glucose metabolism and lipid metabolism (page 4 of the October 17, 2005 Office Action), and it is well known to the skilled artisan that several diseases associated with altered glucose metabolism are accompanied by adverse effects or symptoms such as hyperlipidemia and/or hyperlipoproteinemia. Thus, Applicants have provided an enabling statement, and, under established law, this statement must be taken as enabling unless the Examiner can provide evidence to the contrary. There is no reason to doubt that Applicants’ disclosure is enabling for the described methods. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement made in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367, 370 (CCPA 1971). The Examiner has provided no evidence or reasoning which explains why the Patent Office doubts the truth or accuracy of Applicants’ description of the invention as defined in the pending claims. Furthermore, limitation of coverage to species which have been proven to work or to “preferred” materials, leaves potential avenues for easily circumventing the claims by copiers, and conflicts with the basic purpose of the patent system. *In re Goffe*, 542 F.2d 564, 567, 191 U.S.P.Q. 429, 431 (CCPA 1976).

Applicants maintain that the previously pending claims are enabled throughout their scope. Nevertheless, to expedite prosecution, Applicants have amended claims 109, 112, and 119 to more particularly point out the claimed subject matter. Applicants’ amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection is requested.

Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, and 116-130 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to

enable one of skill in the art to practice the claimed invention. Applicants traverse this rejection to the extent it is maintained in light of the amended claims.

Applicants maintain the arguments of record and contend that the claims are enabled throughout their scope. Nevertheless, to expedite prosecution, Applicants have amended the claims as suggested by the Examiner. Specifically, Applicants have amended the claims to more particularly point out that the instant methods are directed to the use of PYY agonists that have at least two functional properties. PYY agonists for use in some of the presently claimed methods both bind a PYY receptor AND promote glucose-responsiveness of pancreatic islets or pancreatic cells, as recited for example in claims 13, 33, and 45. PYY agonists for use in other of the presently claimed methods both bind a PYY receptor AND alleviate at least one adverse effect or symptom of a disease associated with altered glucose metabolism, as recited for example in claims 21, 23, 88, 89, and 102. Applicants submit that these functional limitations are consistent with the preambles of the respective claims, and are supported by the specification (page 26, lines 19-22, for example). Applicants' amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Applicants' amendments are believed to obviate the rejection, and reconsideration and withdrawal of this rejection are requested.

Additionally, Applicants have cancelled claim 124 as otherwise duplicative of the amended claims.

4. Claim Rejections Under 35 U.S.C. § 103

Claims 23, 89, 102-105, 108, 111, and 118 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over and rendered obvious by Morley *et al.* Applicants traverse this rejection.

Morley *et al.* teach that peripheral administration of PYY to healthy mice results in modest weight loss without altering food intake. The Examiner alleges that the observation of this weight loss in healthy mice would have motivated one of skill in the art to similarly administer PYY to obese mice to promote weight loss. The Examiner further alleges that one of skill in the art would have had a reasonable expectation of success in promoting weight loss in obese mice based on the results of Morley *et al.*

Applicants respectfully disagree with the Examiner's assertions. The teachings of Morley *et al.* fail to satisfy the criteria necessary for rendering the claimed invention obvious. As a first point, the combination of references or teachings must teach or suggest each and every limitation of the claimed invention. In the present case, the claims are directed to methods of treating conditions of altered glucose metabolism. Morley *et al.* fail to teach or suggest that administration of PYY has any effect on glucose metabolism. The Examiner has merely made broad conclusory statements that (i) obesity is a disease associated with altered glucose metabolism and (ii) it would have been obvious to one of skill in the art to modify the method of Morley, *et al.* by administering PYY to obese mice to treat a disease associated with altered glucose metabolism, and that the motivation to do so and the expectation of success is provided by Morley, *et al.* The courts have established that broad conclusory statements regarding the teaching of references standing alone are not 'evidence.' *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999); see also, *In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability, and [can] not be resolved on subjective belief and unknown authority." *In re Sang Su Lee*, 277 F.3d at 1343-44. Absent such evidence, it must be concluded that the Examiner has used impermissible hindsight.

Furthermore, MPEP 2143.01 specifically provides that in establishing a *prima facie* case of obviousness, "the mere fact that references can be combined or modified does not render that resultant combination obvious unless the prior art also suggests the desirability of the combination." Notably, no reason, suggestion or motivation to modify the reference is provided. The courts have also stated that "there must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill . . . would make the combination. That knowledge can not come from the applicant's invention itself." *In re Oetiker*, 977 F.2d 1443, 1447; 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992).

Obesity may be, but is not always, a result of altered glucose metabolism, and a subject of normal weight may suffer from a disease associated with altered glucose metabolism. The skilled artisan would have had to modify the teachings of Morley *et al.* to administer PYY not only to obese mice, but also to a subset of obese animals **having a disease associated with altered glucose metabolism.**

As a second point, a determination of obviousness is not based on what a person skilled in the art might try or find obvious to try. The standard for rendering a claimed invention obvious is that the prior art must suggest to those of ordinary skill in the art that they should have made the claimed invention and that they would have had a reasonable expectation of success in so doing. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In the present case, the Examiner has merely asserted, without evidence, that one of skill in the art would have had a reasonable expectation of success in obtaining similar results with mice having a disease associated with altered glucose metabolism as were obtained with healthy mice. As discussed, Morley *et al.* fail to teach or suggest that PYY causes weight loss, in whole or in part, by altering glucose metabolism. Thus, one of skill in the art would not have had a reasonable expectation of success in using PYY to treat a disease associated with altered glucose metabolism. Additionally, one of skill in the art would readily appreciate that there are physiological and metabolic differences between healthy and diseased animals. There is no basis to assert or assume *a priori* that a treatment having a particular affect on the weight of healthy animals would have a similar impact on the weight of animals having a condition associated with altered glucose metabolism.

At most, in light of Morley *et al.*, administration of PYY to obese animals may have been obvious to try. However, the MPEP and the courts have clearly articulated that obvious to try is not the standard for rendering a claimed invention obvious. MPEP 2143.02; *In re Rinehart*, 531 F.2d 1048 (CCPA 1976); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir. 1991). Prior to Applicants' disclosure, one of skill in the art would not have had a reasonable expectation of success in applying the teachings of Morley *et al.* to the treatment of animals having a disease associated with altered glucose metabolism, as required by the pending claims. Therefore, the Examiner has failed to make a *prima facie* case that Morley *et al.* renders the claimed invention obvious because not all the elements of the claimed invention are found within the teachings of Morley, *et al.*, the reference provides no motivation to modify those teachings, and one of ordinary skill in the art would not have a reasonable expectation of success. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

5. *Claim Rejections Under 35 U.S.C. § 112, second paragraph*

Claims 13, 21, 87, 88, 93, 94, and 102 are rejected under 35 U.S.C. 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants traverse this rejection to the extent it is maintained in light of the amended claims.

Claims 13, 21, 87, 88, 93, and 94 are rejected because recitation of “the pancreatic cell” or “the animal” allegedly undermine the clarity of the claim. To expedite prosecution, Applicants have amended the claims, as suggest by the Examiner, to recite “said pancreatic cell” or “said animal.” Applicants’ amendments are made solely for clarity and do not alter the scope of the claims. Applicants’ amendments are believed to obviate the rejection, and reconsideration and withdrawal of the rejection is requested.

Claim 102 is rejected for allegedly reading on administration of non-effective doses of PYY. To expedite prosecution, Applicants have amended claim 102 to more particularly point out the claimed subject matter. Applicants’ amendment is believed to obviate the rejection, and reconsideration and withdrawal of the rejection is requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under Order No. CIBT-P01-058.**

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Respectfully Submitted,



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